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*Title Page (with full author details)

Risk factors for intraoperative periprosthetic femoral fractures during primary total hip arthroplasty. An analysis from the National Joint Registry for England, Wales and the Isle of Man.

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Risk factors for intraoperative periprosthetic femoral fractures during primary total hip arthroplasty. An analysis from the National Joint Registry for England and Wales.

Abstract:

Background

The aim of this study was to estimate risk factors for intraoperative periprosthetic femoral fractures (IOPFF) and each anatomical subtype (calcar crack, trochanteric fracture, femoral shaft fracture) during primary total hip arthroplasty (THA).

Methods

This retrospective cohort study included 793823 primary THAs between 2004 and 2016. Multivariable regression modelling was used to estimate relative risk of patient, surgical and implant factors for any IOPFF and for all anatomical subtypes of IOPFF. Clinically important interactions were assessed using multivariable regression.

Results

Patient factors significantly increasing the risk of fracture were: female gender, American Association of Anaesthesiologists (ASA) grade 3 to 5, pre-operative diagnosis including: avascular necrosis of the hip (AVN), previous trauma, inflammatory disease, paediatric disease and previous infection. Overall risk of IOPFF associated with age was greatest in patients below 50 years and above 80 years. Risk of any fracture reduced with computer guided surgery (CGS) and in non-NHS hospitals. Non-posterior approach's increased the risk of shaft and trochanteric fracture only. Cementless implants only significantly increased the risk of calcar cracks and shaft fractures and not trochanteric fractures.

Conclusions

Fracture risk increases in patients less than 50 and older than 80, females, ASA grade 3 to 5 and indications other than primary osteoarthritis. Large cumulative reduction in IOPFF risk may occur with use of cemented implants, posterior approach and CGS.

Level of evidence: Level 3b (cohort study).

Key words: Total hip arthroplasty; complications; intraoperative periprosthetic fracture; risk factors

Background:

Total hip arthroplasty (THA) is a highly successful procedure with a low complication rate. Further improvements in outcomes rely on incremental reduction of complications associated with poorer outcomes. One significant complication is intraoperative periprosthetic femoral fracture (IOPFF). IOPFF can occur in the trochanteric region, calcar or femoral diaphysis[1]. Incidence of IOPFF in primary THA ranges from 1–5%[2-4]. Most IOPFF occur during canal preparation and stem implantation [2], when the circumferential strains of the proximal femur are highest[5]. Large strains can occur when the surgeon establishes implant stability through press-fit fixation with cementless femoral implants[6], which increases the risk of IOPFF with cementless femoral implants[2, 3, 7]. IOPFF has been linked to an increased risk of post-operative periprosthetic fracture (PFF) and increased revision risk[2, 8, 9]. Reduced implant survival in cementless implants is perhaps due to failure of primary stability even following adequately treated IOPFF[9].

Prevention of IOPFF by adjusting methods to suit the risk profile of the patient is an obvious means to reduce patient harm and further improve stem survival. Non modifiable risk factors include female sex, increasing age, poor bone quality, abnormal proximal femur morphology[2, 4, 7, 8, 10]. Established modifiable risk factors include cementless stem fixation and surgical approach (direct anterior and Hardinge)[9, 11, 12]. IOPFF is relatively uncommon and previous studies have lacked the size and power to accurately identify other relevant predictors such as computer guided surgery (CGS) or provider organisation type. Current evidence has failed to estimate risk factors for all subtypes of IOPFF. A deeper understanding of how risk factors relate to the specific anatomical subtype of IOPFF will help to develop an understanding of the mechanism by which the increased risk occurs and thus how it can be reduced by future development of approaches, surgical techniques and implants.

The aim was to identify the predictors for all IOPFF, and for each anatomical subtype in the National Joint Registry (NJR) for England and Wales, the largest joint registry in the world.

Materials and Methods:

Database

The NJR has recorded all THAs performed at hospitals in England and Wales since 2003. Patient data and surgical data are collected for each hip arthroplasty. Surgeon-reported IOPFF, have been collected since 1st April 2004. This study included all primary THAs using stemmed implants in the NJR from 1st April 2004 to 30th September 2016.

Participants

793 977 THAs were eligible for analysis. Exclusions were; cases from the Isle of Man (low numbers, n= 153). The resulting subset of data included 793 823 primary THA. Institutional ethical approval was granted and the manuscript was approved by the NJR.

Variables

All variables relating to patient age (years), gender, ASA group (1-2 versus 3-5), year of surgery, side of operation, surgical approach (anterolateral [Hardinge, anterolateral and lateral], trochanteric osteotomy, posterior, other), computer guided surgery (CGS), minimally invasive surgery, surgeon grade (consultant versus non-consultant), hospital type (National Health Service [NHS], Independent hospital, Independent treatment centre), indication (osteoarthritis [OA], trauma including fractured neck of femur [NOF], avascular necrosis [AVN], inflammatory arthritis, previous trauma, paediatric hip disease [congenital dysplasia of the hip, Perthes, skeletal dysplasia, slipped upper femoral epiphysis], malignancy, previous arthrodesis, previous infection and other) and stem fixation type (cemented versus cementless) were included. Year of implantation was used to estimate change in incidence of IOPFF with each subsequent year in the registry dataset (cohort effect).

Outcome

The study outcome was the occurrence of an IOPFF. Reported untoward intraoperative events in the NJR include: “calcar crack”, “shaft fracture”, “shaft penetration”, “trochanteric fracture” and “other”. We included IOPFF as either “calcar crack”, “shaft fracture”, “shaft penetration”, “trochanteric fracture” and text describing IOPFF in “other”. Cases were grouped as calcar, trochanter or shaft fractures (shaft fracture and penetration). Shaft penetration was subsequently dropped because none were recorded.

Statistical analysis:

Analysis was conducted in two parts: firstly, prevalence and risk factors for any IOPFF and secondly prevalence and risk factors for each IOPFF subtype. Univariate comparisons of continuous variables were performed with unpaired t-tests, and comparisons of categorical variables were performed with chi-square tests. Multiple comparison of continuous variables were performed with Pearson x^2 tests. Since the dataset was large and multiple comparisons were made, a significance level of $p < 0.01$ was chosen. A binary multivariable logistic regression model estimated the relative risk (RR) of IOPFF and 95% confidence interval (CI) for each variable compared to normal practice where applicable. The model includes all variables and estimates the individual effect of each variable whilst adjusting for the effects of others and confidence intervals are given to reflect uncertainty of these estimates. In the second part of the analysis, modelling was repeated for fractures of the calcar, shaft and trochanter separately. All analyses were performed using R (v3.5.1, R, Vienna, Austria[13]). Models were assessed using the concordance statistic (C-statistic). Age was determined to be non-linear through fitting of higher order terms, for clarity age was categorised into five groups (<50, 50<60, 60<70, 70<80, 80+ years). Interactions were selected apriori by authors JL and HP and tested by the addition of a single interaction term to the original multivariable models for all IOPFF and each anatomical subtype in turn (Appendix 1). The addition of interaction terms was performed in a single step and repeated for each term. Age was included as a continuous variable to increase accuracy of modelling. The interaction term results of interaction terms on the multivariable models were assessed visually if the interaction term reached statistical significance ($p<0.01$, table 5).

To estimate the overall relative effect of changing all significant modifiable risk factors, comparisons were modelled to calculate the RR (95% CI) of best versus worst practice. The average risk ratio of IOPFF was calculated comparing typical OA hip patients (female, between 60 and 70 years, ASA 1 or 2) undergoing THA with the worst and best selection of modifiable risk factors.

Results:

Part one: All IOPFF

The prevalence of IOPFF during primary THA was 0.62% (4938/793 823). The prevalence of IOPFF more than doubled in patients with cementless compared with cemented femoral implants (0.87% versus 0.42%) ($p<0.001$). Mean age (SD) of patients in the IOPFF group was statistically different to those without IOPFF (68.3 (12.7) years versus 69.2 (11.0) years) ($p<0.001$) although not clinically relevant. IOPFF occurred more commonly in younger (<50) and older (>80) patients. There were a greater proportion of female patients with IOPFF than those without (73.7% versus 61.2%) ($p<0.001$). A greater proportion of patients with IOPFF had a non-OA diagnosis ($p<0.001$) (table 1).

Risk factors for IOPFF

Relative risk of IOPFF almost doubled in females (RR 1.91 (CI 1.79-2.03) (Table 2). Risk of IOPFF increased significantly in the young (age <50, RR 1.21 [CI 1.08-1.37]) and older patients (>80, RR 1.23 [CI 1.14-1.34]) versus patients between 70 and 80 years ($p<0.01$). Risk of IOPFF was 1.08 in left sided THA (CI 1.02-1.14) ($p<0.01$). Risk of IOPFF increased with worse ASA group (3-5) (RR 1.45 [CI 1.35-1.55]). All non-OA indications significantly increased the risk of IOPFF apart from acute trauma and malignancy. Surgical predictors increasing the risk of IOPFF included cementless femoral implants (RR 2.40 [CI 2.26-2.55]) and anterolateral approach (RR 1.09 [CI 1.03-1.16]). Risk of IOPFF was significantly reduced when THA was performed in a non-NHS hospital or when CGS was used (RR 0.51 [CI 0.41-0.65]) ($p<0.01$).

Part two: IOPFF subtypes

Fractures affecting the calcar were most common (n = 3080) (table 3). Calcar cracks occurred more frequently in patients <60 when compared to other fracture types. A smaller proportion of patients with shaft fractures were female when compared to calcar and trochanteric fractures (69.9% versus 72.7% and 77.0%) (p=0.002). Cementless implants were used more commonly in calcar fractures than shaft or trochanteric fractures (73.0% versus 53.7% and 39.8% respectively) (p<0.001).

Risk factors for IOPFF by fracture subtype

Patient factors increasing the risk of IOPFF in each fracture subtype were female gender and ASA grade 3 to 5 (Table 4). Relationship between age and risk of IOPFF varied by fracture subtype (figure 2). Risk of calcar crack significantly increased in the youngest age groups (50<60 [RR 1.18 (1.05-1.31)], <50 [RR 1.52 (CI 1.33-1.75)] p<0.01). Risk of shaft fracture increased significantly in patients over 80 (RR 1.93 [CI 1.47-2.54] p<0.01). Risk of trochanteric fracture increased steadily with age. Indications for THA which increase IOPFF risk for all fracture locations included previous trauma and paediatric disease. Risk of calcar crack also increased for surgical indications including AVN, inflammatory disease, previous infection and “other”. Risk of shaft fracture increased for surgical indications including previous infection and “other”. Risk of trochanteric fracture increased for surgical indication of AVN and inflammatory hip disease.

Cementless implants more than doubled the risk of calcar (RR 3.76 [CI 3.46 – 4.09], p<0.01) and shaft fracture subtypes (RR 2.05 [CI 1.64-2.56], p<0.01). Posterior approach and CGS significantly decreased the risk of shaft fractures and trochanteric fractures.

Interactions between risk factors

The predicted prevalence of any IOPFF increased with cementless stems and worsening ASA group but the prevalence was highest when cementless stems were used (fig 1A). The predicted prevalence of IOPFF on patients with cementless stems was not age dependent and was greater than the prevalence predicted when using a cemented stem although the risk of IOPFF increased with age (fig. 1B). Predicted prevalence of any IOPFF increased with age in patients with OA, whereas patients with a diagnosis of ‘acute trauma including NOF’ and ‘other’ were predicted to experience an inverse relationship, with higher prevalence of any IOPFF in younger age groups (fig. 1C). The relationship between age and diagnosis remained consistent to the overall effect when patients underwent surgery for OA (fig. 1D, left). Patients with a diagnosis of ‘other’ were predicted higher prevalence of any IOPFF when using cemented and cementless stems in younger age groups and the prevalence of any

IOPFF decreased in older patients (fig. 1D, right). The predicted prevalence of calcar crack increased in females versus males and in cementless versus cemented stem but the effect of cementless stems on risk of calcar crack was much larger for females than males (fig. 1E). The predicted prevalence of calcar cracks increased in younger patients in those undergoing THA with cementless stems, whereas the predicted prevalence of calcar cracks with cemented stems was consistently low across the age range of patients in the study (fig. 1F). The predicted prevalence of shaft fracture was much increased in older females, whereas the predicted prevalence of shaft fracture remained consistently low across all ages with cemented implants (fig. 1G). The predicted prevalence of trochanteric fracture was higher in younger patients when THA was performed for acute trauma including NOF in comparison to THA performed for osteoarthritis (fig. 1H). Predicted prevalence of trochanteric fracture was highest in consultants performing ‘other’ approaches compared to non-consultants using the same approach, whereas predicted prevalence of trochanteric fracture was roughly equivalent between lead surgeon grades using other approaches (fig. 1I). The fixed effects of statistically significant interactions are given in table 5.

Effects of combined predictors

Combined relative risk of shaft IOPPF was 7.49 (CI 2.78 - 20.02) when using the worst (cementless stem via “other” or Anterolateral approach without CGS) versus the best (cemented stem via posterior approach with CGS) selection of modifiable risk factors when operating on a typical OA hip patient (table 5) ($p<0.01$).

Discussion:

This paper is the largest study reporting risk factors for IOPFF subtypes during primary THA. It outlines new risk factors for IOPFF which can be used to identify and protect patients undergoing THA. Risk of IOPFF is highest at extremes of age and not just the older patient population. Higher preoperative ASA grade is associated with increased risk of IOPFF. IOPFF risk did not rise in hip fracture but did increase in all other non-OA diagnoses. Cementless stem use is associated with increased risk of calcar and shaft fractures. Cementless stems appear to be an age independent risk factor for any IOPFF. Anterolateral and ‘other’ approaches can increase the risk of trochanteric and shaft fractures versus posterior approach. Computer guided surgery reduced risk of any IOPFF and its effect appeared to affect all patients consistently. With judicious adjustment of modifiable risk factors, a potential seven-fold reduction in relative risk of IOPFF may be achieved.

Patient related risk factors for IOPFF

The risk of IOPFF approximately doubles in females[2, 4, 8, 14]. These results have shown an increasing predicted prevalence of shaft fracture with increasing age in females, but no other interaction effect of age on gender in other anatomical subtypes. Gender differences and gender-age interactions may exist because females are affected by post-menopausal osteoporosis which reduces bone strength[15]. The greatest age associated risk was seen in both patients below 50 years and above 80 years old. Prevalence of any IOPFF increased in younger patients with acute fracture and ‘other’ indications relative to patients with OA. Increasing age has been previously associated with higher IOPFF fracture risk[2, 4]. Young patients may be at greater risk of calcar and shaft fractures because the proximal femoral canal is typically tighter and requires more prolonged and forceful rasping. Many young patients requiring hip replacement have dysplastic proximal femora which may be particularly narrow or osteoporotic. The risk of trochanteric fracture increased with age in patients with OA but analysis of interactions demonstrated that the predicted prevalence of trochanteric fracture decreased with age to below that of OA in older patients with a diagnosis of acute fracture including NOF. Given that the metaphyseal bone of the trochanter is particularly vulnerable to osteoporosis, it is not clear why this might be observed. Perhaps increased surgeon awareness of osteoporosis in patients with NOF may reduce the risk of trochanteric injury.

Patients undergoing left sided THA have an 8% increased risk of IOPFF ($p<0.001$) (table 2). This could be due to surgeon handedness, which has been shown to affect surgical performance during THA[16].

Inflammatory arthritis, previous trauma and NOF are commonly associated with periarticular osteoporosis and increased risk of IOPFF. This study did not find increased risk of IOPFF with THA for NOF, which is a surprising finding. Patients with NOF are typically older and perhaps more likely to have a wider proximal femoral canal, which reduces femoral stem mismatch. This study confirmed that AVN, previous trauma and previous infection were associated with a significant increase in IOPFF risk[4]. Exposure to steroids, associated osteopenia and / or post-operative bone loss or fibrosis may make exposure and femoral canal preparation precarious. Worse ASA grade is strongly associated with increased IOPFF risk. ASA is likely to be a surrogate marker for health conditions which can affect the integrity of the proximal femoral bone stock. ASA grade may be a useful discriminator for surgeons deciding which implants and techniques to adopt.

Surgery / surgeon related risk factors for IOPFF

Increased relative risk of IOPFF associated with cementless implant usage is reflected universally in the literature [2, 3, 8-10, 17, 18]. We have demonstrated that the effect of cementless stem use resulted in a constant elevated predicted prevalence of any IOPFF across all age ranges. Associated risk of calcar and shaft fractures also independently increased with cementless stem use. Calcar or shaft fractures tend to occur during canal preparation and stem insertion[2] where most cementless femoral implants use a press fit which increases femoral cortical strains[6]. The increased risk of calcar crack associated with cementless stems was most noticeable in female patients and there was no significant age-gender interaction when predicting calcar cracks. It is possible that there are gender differences between the morphology of female and male proximal femurs which may predispose female to calcar cracks during cementless stem implantation but there is little evidence to support this observation.

Cementless stem survival has previously been shown to be better in a younger population of patients perhaps because of better bone stock which reduces the risk of perioperative complications like IOPFF and PFF[19]. In younger patients where it has been shown that cementless femoral stems may survive longer the increased risk of IOPFF and associated sequelae must be weighed up against the potential benefit in stem survival, particularly in patients with proximal femoral features appear weak or which may require prolonged or forceful preparation. The decision to use cementless or a cemented stem is complex and given that risk of IOPFF increased in the youngest patients in this study perhaps surgeons and policy makers should use other standardised variables to identify groups in which survival with cementless stems is better.

Surgical approach to the hip is a contentious topic with rising popularity of the direct anterior approach because of potentially reduced dislocation rates and faster recovery. Hardinge approach has previously been identified as a risk factor for IOPFF[8, 9, 11, 17]. The Hardinge and direct anterior approach can place significant forces on trochanteric muscle attachments and the femur, which are under tension during canal preparation and implantation[11, 12]. Increased rotational loading of the trochanter and shaft during anterolateral and other approaches may explain the specific increased risk of IOPFF. These results predicted that consultant surgeons experienced a higher prevalence of trochanteric fractures during ‘other’ approaches compared to non-consultant grade surgeons. This is likely to be the result of selection bias, with consultant surgeons electing to perform ‘other’ approaches on more challenging cases. The absolute predicted risk of consultant lead surgeons performing ‘other’ approaches was higher than any other group and highlights the particular risk associated with these approaches. Further work to adapt these approaches to reduce femoral strains may help to reduce associated risk of IOPFF.

This is the first study to demonstrate an association between CGS and a reduced risk of any IOPFF, calcar and trochanteric subtypes. CGS typically requires pre-operative 3D imaging, which may allow more accurate planning of implant size and can give feedback on direction of femoral preparation and implantation. There were no clinically plausible interactions between CGS and other variables in this study. This may suggest that CGS is an independent protective factor against any IOPFF. However, confounding may exist since CGS may also be a surrogate marker for careful higher volume surgeons and surgeons may select easier or more difficult cases for CGS assistance. We identified higher incidence of IOPFF in patients undergoing surgery in public hospitals. In the UK surgery undertaken in independent hospital are more likely to be performed by consultant surgeons and patients tend to be fitter and cases less complex which may introduce confounding. Although the overall risk of IOPFF seems low, the surgeon is able to reduce the risk significantly further by modifying all possible risk factors which they have control over.

This observational study benefits from the power of large numbers which can give insight into relatively rare complications but are constrained by the innate availability of data. There are important risk factors which cannot be included such as proximal femoral morphology, proximal femoral bone mineral density, specific implant/rasp design and shape, force of impaction and control over surgical techniques. Given this constraint, the performance of models used in this study are adequate but results should be appraised alongside other data. NJR IOPFF data are self-reported immediately after surgery and may miss shaft fractures which are only seen on post-operative radiographs. This may explain why there are no reported shaft penetrations in this study. Abdel *et al[2]* reported 5.6% of all IOPFF were shaft fractures and 24% of these were discovered on post-operative radiographs. In this study shaft IOPFF accounted for 7.1 % of all IOPFF, but this may be an underestimate given these limitations. Cementless femoral implants may be used preferentially in cases of IOPFF if the surgeon prefers to use a cementless distally fixing modular implant, which may bias results. However, cementless modular implants were used in only 3.2% of all the IOPFF in our analysis, which could introduce only a small error into our estimates of the effect of fixation. Not all variables identified in multivariable regression were selected using the ctree analysis. This is likely to be because ctree analysis was performed on a smaller and smaller subgroup reducing the likelihood of a relatively infrequently occurring variable being selected by the algorithm. The analysis of stem properties associated with intraoperative fracture is not feasible as the NJR only records the final implant used and not the precise preparation equipment (rasps and or reamers) used. It is likely that the numbers reported here are an underestimate of IOPPF as the fractures are only reported if the surgeon is aware of their occurrence during surgery.

Conclusions

The risk of all IOPFF increases in females, less fit patients and in those with a non-OA indication for surgery. Large cumulative reduction in IOPFF risk appears associated with use of cemented implants, posterior approach and CGS. Understanding the effect of combined factors is paramount when choosing the safest technique and implant choice to minimise IOPFF and future revision risk. Future work should elucidate the effect of CGS as well as direct anterior approach on the risk of IOPFF given that there are significant effects of CGS and the use of direct anterior approach is increasing. Although there is some evidence to suggest a link between IOPFF and poorer implant survival, further analysis to assess the impact of IOPFF subtypes on patient and implant survival is required.

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Table 1. Summary descriptive statistics for primary total hip arthroplasty with and without IOPFF during primary surgery

	No IOPFF	IOPFF	p overall
Side			0.010
Left	355794 (45.10%)	2318 (46.94%)	
Right	433091 (54.90%)	2620 (53.06%)	
Gender			<0.001*
Female	482627 (61.18%)	3644 (73.80%)	
Male	306258 (38.82%)	1294 (26.20%)	
Age group			<0.001*
11 to 49	39044 (4.95%)	401 (8.12%)	
50 to 59	97113 (12.31%)	693 (14.03%)	
60 to 69	235370 (29.84%)	1346 (27.26%)	
70 to 79	283522 (35.94%)	1567 (31.73%)	
80 to 117	133836 (16.97%)	931 (18.85%)	
ASA group			<0.001*
1 and 2	663279 (84.08%)	3857 (78.11%)	
3 to 5	125606 (15.92%)	1081 (21.89%)	
Indication			<0.001*
Osteoarthritis	728589 (92.36%)	4194 (84.93%)	
Acute trauma including hip fracture	22003 (2.79%)	148 (3.00%)	
Avascular necrosis	10476 (1.33%)	123 (2.49%)	
Previous trauma	7116 (0.90%)	174 (3.52%)	
Inflammatory arthritis	8559 (1.08%)	102 (2.07%)	
Malignancy	324 (0.04%)	3 (0.06%)	
Other	5841 (0.74%)	68 (1.38%)	
Paediatric disease	5301 (0.67%)	111 (2.25%)	
Previous arthrodesis	242 (0.03%)	2 (0.04%)	
Previous infection	434 (0.06%)	13 (0.26%)	
Stem fixation			<0.001*
Cemented	444464 (56.34%)	1901 (38.50%)	
Cementless	344421 (43.66%)	3037 (61.50%)	
Lead surgeon grade			0.895
Consultant	651974 (82.64%)	4077 (82.56%)	
Non consultant	136911 (17.36%)	861 (17.44%)	
Organisation type			<0.001*
NHS	538645 (68.28%)	3813 (77.22%)	
Independent hospital	217267 (27.54%)	999 (20.23%)	
Treatment centre	32973 (4.18%)	126 (2.55%)	
Approach			0.002*
Posterior	454410 (57.60%)	2721 (55.10%)	
Anterolateral	297413 (37.70%)	1967 (39.83%)	
Trochanteric Osteotomy	3017 (0.38%)	14 (0.28%)	
Other	34045 (4.32%)	236 (4.78%)	
Surgical technique			
Minimally invasive surgery			1.000
No	734071 (93.05%)	4595 (93.05%)	
Yes	54814 (6.95%)	343 (6.95%)	
Computer guided surgery			<0.001*
No	767299 (97.26%)	4857 (98.36%)	
Yes	21586 (2.74%)	81 (1.64%)	

Note: Results are numbers (% of column within group). ASA denotes American society of Anaesthesiologists grade, NHS is National Health Service. *p<0.01.

Table 2. Results from multivariable regression demonstrating risk factors for any IOPFF during primary total hip arthroplasty

	Relative risk of IOPFF (95% confidence interval)
Side	
Left	1.08 (1.02 - 1.14)*
Right	1
Gender	
Female	1.91 (1.79 - 2.03)*
Male	1
Age group	
11 to 49	1.21 (1.08 - 1.37)*
50 to 59	1.05 (0.95 - 1.15)
60 to 69	0.94 (0.87 - 1.01)
70 to 79	1
80 to 117	1.23 (1.14 - 1.34)*
ASA group	
1 and 2	1
3 to 5	1.45 (1.35 - 1.55)*
Indication	
Osteoarthritis	1
Acute trauma including hip fracture	1.13 (0.96 - 1.34)
Avascular necrosis	1.81 (1.51 - 2.17)*
Previous trauma	3.80 (3.27 - 4.42)*
Inflammatory arthritis	1.75 (1.44 - 2.13)*
Malignancy	2.01 (0.65 - 6.22)
Other	1.85 (1.45 - 2.35)*
Paediatric disease	2.78 (2.28 - 3.38)*
Previous arthrodesis	1.25 (0.31 - 4.96)
Previous infection	4.92 (2.88 - 8.40)*
Stem fixation	
Cemented	1
Cementless	2.40 (2.26 - 2.55)*
Lead surgeon grade	
Consultant	1
Non consultant	0.96 (0.89 - 1.04)
Organisation type	
NHS	1
Independent hospital	0.68 (0.63 - 0.73)*
Treatment centre	0.58 (0.49 - 0.70)*
Approach	
Posterior	1
Anterolateral	1.09 (1.03 - 1.16)*
Trochanteric Osteotomy	0.97 (0.57 - 1.63)
Other	1.08 (0.94 - 1.23)
Surgical technique	
Minimally invasive surgery	0.98 (0.87 - 1.10)
Computer guided surgery	0.51 (0.41 - 0.65)*
Cohort effect	
Subsequent year of primary surgery	0.97 (0.96 - 0.97)*
Observations	793,823
C - statistic	0.68

Note: Results are relative risks (95% confidence intervals). ASA denotes American society of Anaesthesiologists grade, NHS is National Health Service. *Ins* denotes insufficient numbers for meaningful analysis. *p<0.01

Table 3. Summary descriptive statistics for primary total hip arthroplasty with and without IOPFF subtypes during primary surgery

	Calcar cracks n = 3080	Shaft fractures n = 352	Trochanteric fractures n = 1506	p overall
Side				0.980
Left	1444 (46.88%)	167 (47.44%)	707 (46.95%)	
Right	1636 (53.12%)	185 (52.56%)	799 (53.05%)	
Gender				0.002*
Female	842 (27.34%)	106 (30.11%)	346 (22.97%)	
Male	2238 (72.66%)	246 (69.89%)	1160 (77.03%)	
Age group				<0.001*
11 to 49	330 (10.71%)	28 (7.95%)	43 (2.86%)	
50 to 59	511 (16.59%)	30 (8.52%)	152 (10.09%)	
60 to 69	899 (29.19%)	82 (23.30%)	365 (24.24%)	
70 to 79	906 (29.42%)	106 (30.11%)	555 (36.85%)	
80 to 117	434 (14.09%)	106 (30.11%)	391 (25.96%)	
ASA group				<0.001*
1 and 2	2534 (82.27%)	251 (71.31%)	1072 (71.18%)	
3 to 5	546 (17.73%)	101 (28.69%)	434 (28.82%)	
Indication				0.001*
Osteoarthritis	2630 (85.39%)	280 (79.55%)	1284 (85.26%)	
Acute trauma including hip fracture	86 (2.79%)	11 (3.12%)	51 (3.39%)	
Avascular necrosis	84 (2.73%)	6 (1.70%)	33 (2.19%)	
Previous trauma	92 (2.99%)	30 (8.52%)	52 (3.45%)	
Inflammatory arthritis	54 (1.75%)	8 (2.27%)	40 (2.66%)	
Malignancy	1 (0.03%)	0 (0.00%)	2 (0.13%)	
Other	43 (1.40%)	7 (1.99%)	18 (1.20%)	
Paediatric disease	80 (2.60%)	8 (2.27%)	23 (1.53%)	
Previous arthrodesis	1 (0.03%)	0 (0.00%)	1 (0.07%)	
Previous infection	9 (0.29%)	2 (0.57%)	2 (0.13%)	
Stem fixation				<0.001*
Cemented	831 (26.98%)	163 (46.31%)	907 (60.23%)	
Cementless	2249 (73.02%)	189 (53.69%)	599 (39.77%)	
Lead surgeon grade				<0.001*
Consultant	2601 (84.45%)	294 (83.52%)	1182 (78.49%)	
Non consultant	479 (15.55%)	58 (16.48%)	324 (21.51%)	
Organisation type				<0.001*
NHS	2278 (73.96%)	262 (74.43%)	1273 (84.53%)	
Independent hospital	713 (23.15%)	80 (22.73%)	206 (13.68%)	
Treatment centre	89 (2.89%)	10 (2.84%)	27 (1.79%)	
Approach				<0.001*
Posterior	1839 (59.71%)	160 (45.45%)	722 (47.94%)	
Anterolateral	1109 (36.01%)	164 (46.59%)	694 (46.08%)	
Trochanteric Osteotomy	8 (0.26%)	2 (0.57%)	4 (0.27%)	
Other	124 (4.03%)	26 (7.39%)	86 (5.71%)	
Surgical technique				
Minimally invasive surgery				0.002*
Yes	244 (7.92%)	20 (5.68%)	79 (5.25%)	
No	2836 (92.08%)	332 (94.32%)	1427 (94.75%)	
Computer guided surgery				0.723
Yes	3026 (98.25%)	347 (98.58%)	1484 (98.54%)	
No	54 (1.75%)	5 (1.42%)	22 (1.46%)	

Note: Results are numbers (% of column within group). ASA denotes American society of Anaesthesiologists grade, NHS is National Health Service. *p<0.01.

Table 4. Results from multivariable regression demonstrating risk factors for IOPFF subtypes

	Relative risk (95% confidence interval)		
	Calcar cracks	Shaft fractures	Trochanteric fractures
Side			
Left	1.07 (1.00 - 1.15)	1.09 (0.88 - 1.34)	1.10 (0.99 - 1.22)
Right	1	1	1
Gender			
Female	1.91 (1.76 - 2.06)*	1.46 (1.16 - 1.84)*	2.06 (1.82 - 2.32)*
Male	1	1	1
Age group			
11 to 49	1.52 (1.33 - 1.75)*	1.30 (0.82 - 2.05)	0.46 (0.33 - 0.64)*
50 to 59	1.18 (1.05 - 1.31)*	0.71 (0.47 - 1.07)	0.83 (0.69 - 0.99)
60 to 69	1.00 (0.91 - 1.09)	0.88 (0.66 - 1.18)	0.84 (0.73 - 0.96)
70 to 79	1	1	1
80 to 117	1.09 (0.97 - 1.22)	1.93 (1.47 - 2.54)*	1.29 (1.13 - 1.47)*
ASA group			
1 and 2	1	1	1
3 to 5	1.27 (1.16 - 1.40)*	1.79 (1.40 - 2.29)*	1.69 (1.50 - 1.90)*
Indication			
Osteoarthritis	1	1	1
Acute trauma including hip fracture	1.25 (1.00 - 1.55)	1.26 (0.68 - 2.32)	0.95 (0.72 - 1.26)
Avascular necrosis	1.85 (1.48 - 2.31)*	1.35 (0.60 - 3.08)	1.89 (1.33 - 2.68)*
Previous trauma	3.63 (2.95 - 4.46)*	9.01 (6.14 - 13.24)*	3.09 (2.34 - 4.08)*
Inflammatory arthritis	1.47 (1.13 - 1.93)*	2.21 (1.09 - 4.50)	2.30 (1.68 - 3.16)*
Malignancy	1.42 (0.20 - 10.05)	*ins*	2.97 (0.74 - 11.90)
Other	1.87 (1.38 - 2.53)*	2.82 (1.32 - 6.00)*	1.61 (1.01 - 2.56)
Paediatric disease	2.58 (2.04 - 3.25)*	3.75 (1.76 - 7.95)*	3.58 (2.32 - 5.53)*
Previous arthrodesis	0.94 (0.13 - 6.62)	*ins*	2.24 (0.32 - 15.84)
Previous infection	5.27 (2.76 - 10.05)*	12.00 (2.97 - 48.58)*	2.87 (0.72 - 11.48)
Stem fixation			
Cemented	1	1	1
Cementless	3.76 (3.46 - 4.09)*	2.05 (1.64 - 2.56)*	1.13 (1.02 - 1.26)
Lead surgeon grade			
Consultant	1	1	1
Non consultant	0.96 (0.86 - 1.06)	0.89 (0.67 - 1.20)	0.98 (0.86 - 1.11)
Organisation type			
NHS	1	1	1
Independent hospital	0.77 (0.70 - 0.84)*	0.91 (0.70 - 1.19)	0.46 (0.40 - 0.54)*
Treatment centre	0.63 (0.51 - 0.79)*	0.82 (0.43 - 1.55)	0.41 (0.28 - 0.60)*
Approach			
Posterior	1	1	1
Anterolateral	0.94 (0.87 - 1.02)	1.54 (1.23 - 1.93)*	1.36 (1.22 - 1.51)*
Trochanteric Osteotomy	1.03 (0.51 - 2.05)	2.03 (0.51 - 8.16)	0.77 (0.29 - 2.05)
Other	0.83 (0.69 - 1.00)	2.06 (1.36 - 3.12)*	1.51 (1.21 - 1.89)*
Surgical technique			
Minimally invasive surgery	1.01 (0.88 - 1.16)	0.82 (0.50 - 1.32)	0.92 (0.72 - 1.18)
Computer guided surgery	0.53 (0.40 - 0.71)*	0.49 (0.19 - 1.25)	0.48 (0.31 - 0.76)*
Cohort effect			
Subsequent year of primary	0.96 (0.95 - 0.97)*	0.96 (0.93 - 0.99)	0.98 (0.97 - 1.00)
Observations	791,965	788,671	790,391
C - statistic	0.71	0.69	0.68

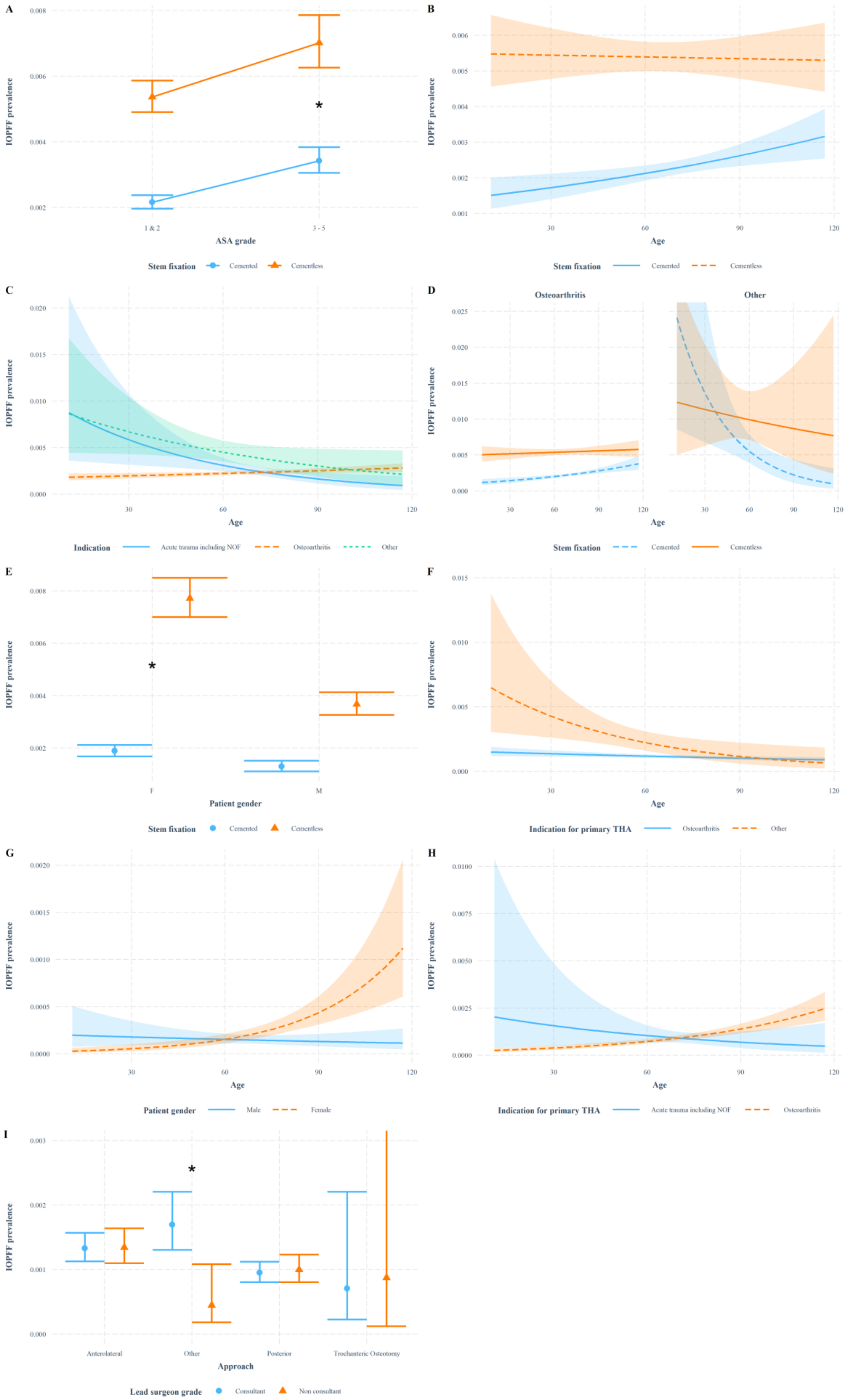
Note: Results are relative risks (95% confidence intervals). ASA denotes American society of Anaesthesiologists grade, NHS is National Health Service. *Ins* denotes insufficient numbers for meaningful analysis. *p<0.01

Table 5. Fixed effects of statistically singnificant interaction terms.

Multivariable model outcome	Interaction covariates	Interaction level	RR	p
Any IOPFF	ASA : Fixation	ASA grade 3 to 5 : Cementless stem	0.83	<0.01
Any IOPFF	Age : Fixation	Age increase of one year : Cementless stem	0.99	<0.01
Any IOPFF	Age : Indication	Age increase of one year : Acute trauma including NOF	0.96	<0.01
Any IOPFF	Age : Indication	Age increase of one year : Other	0.96	<0.01
Any IOPFF	Age : Indication : Fixation	Age increase of one year : Other: Cementless stem	0.08	<0.01
Calcar crack	gender : Fixation	Female gender : Cementless stem	1.44	<0.01
Calcar crack	Age : Indication	Age increase of one year : Other	0.96	<0.01
Shaft fracture	Age : Gender	Age increase of one year : Female gender	1.04	<0.01
Trochanteric fracture	Age : Indication	Age increase of one year : Acute trauma including NOF	0.95	<0.01
Trochanteric fracture	leadsurgeon : approach	Non Consultant : Other	0.25	<0.01

Note: IOPFF indicates intraoperative periprosthetic femoral fracture, RR indicates relative risk associated with interaction term, p indicates the significance of the interaction term in the multivariable model indicated in IOPFF type, THA indicates total hip arthroplasty, CGS indicates computer guided surgery, ASA indicated American society of anaesthesiologists and NOF indicates neck of femur fracture

Figure 1: Panel plot demonstrating effect of significant interaction terms on the predicted incidence of intraoperative periprosthetic femoral fracture during primary total hip arthroplasty.


A
IOPFF prevalence
ASA grade
1 & 2
3 - 5
Stem fixation
Cemented
Cementless
B
IOPFF prevalence
Age
Stem fixation
Cemented
Cementless
C
IOPFF prevalence
Age
Indication
Acute trauma including NOF
Osteoarthritis
Other
D
Osteoarthritis
Other
IOPFF prevalence
Age
Stem fixation
Cemented
Cementless
E
IOPFF prevalence
Patient gender
F
M
Stem fixation
Cemented
Cementless
F
IOPFF prevalence
Age
Indication for primary THA
Osteoarthritis
Other
G
IOPFF prevalence
Age
Patient gender
Male
Female
H
IOPFF prevalence
Age
Indication for primary THA
Acute trauma including NOF
Osteoarthritis
I
IOPFF prevalence
Approach
Anterolateral
Other
Posterior
Trochanteric Osteotomy
Lead surgeon grade
Consultant
Non consultant

Note: Figure 1(A) Demonstrates the interaction of ASA grade and stem fixation on risk of IOPFF risk. Figure 1(B) demonstrates the interaction of patient age and stem fixation on predicted prevalence of any IOPFF.

Figure 1(C) Demonstrates the interaction of patient age and indication for primary surgery on predicted prevalence of anyIOPFF. only diagnoses which reached statistical significance and osteoarthritis (reference) are displayed.

Figure 1(D) Demonstrates the interaction of patient age, indication for primary surgery and stem fixation on predicted prevalence of any IOPFF. only diagnoses which reached statistical significance and osteoarthritis (reference) are displayed.

Figure 1(E) Demonstrates the interaction of patient gender and stem fixation on predicted prevalence of calcar crack.

Figure 1(F) Demonstrates the interaction of patient age and indication for surgery on predicted prevalence of calcar crack. only diagnoses which reached statistical significance and osteoarthritis (reference) are displayed.

Figure 1(G) Demonstrates the interaction of patient age and gender on predicted prevalence of shaft fracture.

Figure 1(H) Demonstrates the interaction of patient age and indication for surgery on predicted prevalence of trochanteric fracture.

Figure 1(I) Demonstrates the interaction of lead surgeon grade and surgical approach on predicted prevalence of trochanteric fracture.

* denotes the level of categorical variable at which the interaction reaches significance

Table 6. Relative risk of IOPFF in a typical OA patient undergoing THA using a selection of worst vs best modifiable risk factors.

Fracture type	RR	(95% CI)	p
All fractures	4.29	(3.34 - 5.51)	<0.001*
Calcar crack	7.72	(5.65 - 10.50)	<0.001*
Shaft fracture	2.93	(1.17 - 7.32)	0.02
Trochanteric	1.64	(1.02 - 2.64)	0.042

Note: Best scenario (Cemented stem, posterior approach and computer guided surgery), worst scenario (Cementless stem, Anterolateral or other approach without computer guided surgery. RR Relative risk, CI confidence interval, * p<0.01

Appendix

A.1:

A priori clinically relevant interactions tested
age : gender
gender : stem sixation
ASA : stem sixation
ASA : lead surgeon grade
ASA : lead surgeon grade : stem sixation
age : stem sixation
age : gender : stem sixation
age : indication
age : indication : stem sixation
cgs : age
cgs : indication
cgs : age : indication
cgs : side
cgs : lead surgeon grade
cgs : approach
cgs : stem sixation
cgs : stem sixation : organisation type
lead surgeon grade : organisation
lead surgeon grade : approach
side : approach *
side : surgeon *
side : surgeon : approach *

Note: THA indicates total hip arthroplasty, CGS indicates computer guided surgery, ASA indicated American society of anaesthesiollogists. * denotes interaction only tested on multivariable model predicting risk of any intraoperative fracture